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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
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ART UNIT	PAPER NUMBER
1642	9

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/559,874	Applicant(s) LENG, JAY	
	Examiner Stephen L. Rawlings, Ph.D.	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-70* is/are pending in the application.

4a) Of the above claim(s) *48-62,69 and 70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-48 and 63-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-70* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment filed on September 14, 2001 in Paper No. 8 is acknowledged and has been entered. Claims 1, 18, 31, and 63 are amended.

2. Claims 1-70 are pending in the application. Claims 48-62, 69, and 70 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim. The election in Paper No. 6 was treated as an election made without traverse for the reason stated in the previous Office Action (Paper No. 7).

3. Claims 1-47 and 63-68 are currently under prosecution.

Specification

4. As stated in the previous Office Action, the disclosure is objected to because on page 14 the ATCC accession is omitted.

In Paper No. 8 Applicant acknowledge the objection and state, "[u]nder 37 CFR 1.809(b)(1), a deposit is required on or before the date of payment of the issue fee." (page 5, paragraph 1). Applicant further states that the deposit will be made and the number will be inserted on or before the payment of the issue fee.

In response to Applicant's statements, it is noted that 37 CFR § 1.809 reads as follows:

> (a) The examiner shall determine pursuant to § 1.104 in each application for patent, application for reissue patent or reexamination proceeding if a deposit is needed, and if needed, if a deposit actually made is acceptable for patent purposes. If a deposit is needed and has not been made or replaced or supplemented in accordance with these regulations, the examiner, where appropriate, shall reject the affected claims under the appropriate provision of 35 U.S.C. 112, explaining why a deposit is needed and/or why a deposit actually made cannot be accepted.
>
> (b) The applicant for patent or patent owner shall reply to a rejection under paragraph (a) of this section by—
>
> (1) In the case of an applicant for patent, either making an acceptable original, replacement, or supplemental deposit, or assuring the Office in writing that an

> acceptable deposit will be made; or, in the case of a patent owner, requesting a certificate of correction of the patent which meets the terms of paragraphs (b) and (c) of § 1.805, or
>
> (2) Arguing why a deposit is not needed under the circumstances of the application or patent considered and/or why a deposit actually made should be accepted. Other replies to the examiner's action shall be considered nonresponsive. The rejection will be repeated until either paragraph (b)(1) of this section is satisfied or the examiner is convinced that a deposit is not needed.
>
> (c) If an application for patent is otherwise in condition for allowance except for a needed deposit and the Office has received a written assurance that an acceptable deposit will be made, applicant will be notified and given a period of time within which the deposit must be made in order to avoid abandonment. This time period is not extendable under § 1.136(a) or (b) if set forth in a "Notice of Allowability" or in an Office action having a mail date on or after the mail date of a "Notice of Allowability" (see § 1.136(c)).
>
> (d) For each deposit made pursuant to these regulations, the specification shall contain:
>
> (1) The accession number for the deposit;
>
> (2) The date of the deposit;
>
> (3) A description of the deposited biological material sufficient to specifically identify it and to permit examination; and
>
> (4) The name and address of the depository.
>
> (e) Any amendment required by paragraphs (d)(1), (d)(2) or (d)(4) of this section must be filed before or with the payment of the issue fee (see § 1.312).
>
> [Added, 54 FR 34882, Aug. 22, 1989, effective Jan. 1, 1990; paras. (b) and (c) revised and para. (e) added, 66 FR 21092, Apr. 27, 2001, effective May 29, 2001]

Accordingly, it is noted that the Examiner did not require that the deposit be made; rather, it is the specification that indicates that a deposit *has been made* at or before the time of the filing date currently sought by Applicant (page 14, lines 8-12). While the specification remains incomplete for the omission of the ATCC accession number, it is further noted that the claims drawn to the elected invention are not affected by the omission of the ATCC accession number from the specification. In this regard, 37 CFR § 1.809 is not strictly applicable to the stated grounds of objection. Therefore, the objection to the specification is maintained.

However, in view of Applicant's expressed willingness to make the deposit and to amend the specification to insert the ATCC accession number, this matter will be set aside until this application is in a condition for allowance except for the needed deposit and amendment to the specification. At that time Applicant will be invited make the deposit and amend the specification. Applicant will be given a period of time within which the deposit must be made in order to avoid

abandonment. This time period is not extendable under § 1.136(a) or (b) if set forth in a "Notice of Allowability" or in an Office action having a mail date on or after the mail date of a "Notice of Allowability" (see § 1.136(c)).

5. In response to the previous Office Action, it is noted that the amendment to the specification corrects the misspelling of "coelenterazine" and thus obviates part of the basis of objection to the specification.

Claim Rejections Withdrawn

6. In response to the previous Office Action, claim 63 has been amended to more particularly point out and distinctly claim the subject matter that Applicant regard as the invention. In particular, the amendment to the claim better relates the difference in the cell's light emissions in the presence and absence of the agent to the cell's susceptibility to treatment with the agent. Accordingly, the rejection of claims 63-68 under 35 USC § 112, second paragraph for the reason set forth in the last paragraph of section 8 of the previous Office Action is withdrawn.

Claim Rejections Maintained and Response to Applicant' Remarks

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-47 and 63-68 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

With regard to the first paragraph of section 5 in the previous Office Action, it is noted that claims 31-47 were inadvertently not included in the list of claims rejected under 35 USC § 112, first paragraph. However, claims 31-47 were included in the claims analysis of the following paragraph and the claims were further addressed in the grounds of rejection. Therefore, it is obvious that claims 31-47 were meant to be included in the list of the rejected claims.

Claims 1-17 are drawn to an *in vitro* method for determining the effect of an agent on cell proliferation, said method comprising contacting a cell containing a *Renilla* luciferase polypeptide or a polynucleotide encoding a *Renilla* luciferase with an agent suspected of modulating cell proliferation and comparing the light emission data from the cell in the presence of the agent to the light emission data from the cell in the absence of the agent. Claims 18-30 are drawn to an *in vitro* method for determining cell proliferation of a cell or population of cells, said method comprising obtaining light emission data from the cell or population of cells, which contain a *Renilla* luciferase polypeptide or a polynucleotide encoding a *Renilla* luciferase, over a period of time wherein a change in light emission data is indicative of a corresponding change in cell proliferation. Claims 31-47 are drawn to an *in vitro* method for determining the effect of an agent on cell proliferation, said method comprising transfecting a cell obtained from a sample with a vector encoding *Renilla* luciferase, contacting the transfected cell with the agent, and comparing the light emission data from the cell in the presence of the agent to the light emission data from the cell in the absence of the agent, wherein a difference in light emission data is indicative of an effect on cell proliferation. Claims 63-68 are drawn to an *in vitro* or an *in vivo* method of screening mammalian cells to determine their susceptibility to treatment with an agent, said method comprising contacting the cells, which contain a *Renilla* luciferase polypeptide or a polynucleotide encoding a *Renilla* luciferase, and measuring light emissions from the cells in the presence and absence of the agent, wherein a difference in light emissions is indicative of the cells' susceptibility to treatment with the agent.

The grounds of rejection were stated in section 5 of the previous Office Action. Essentially, claims 1-47 and 63-68 are rejected under 35 USC § 112, first paragraph because the teachings of the specification cannot be extrapolated to the enablement of the claimed invention. In particular, there is insufficient guidance in the specification and working exemplification of the invention is not commensurate in scope with the claims. Therefore, because of the high level of unpredictability in the art, one skilled in the art cannot practice the claimed invention with a reasonable expectation of success without first performing undue experimentation.

Applicant traverses the rejection of claims 1-47 and 63-68 under 35 US C§ 112, first paragraph and argues, "one of skill in the art would have known, at the time of filing of the application, using the teachings of the application, how to practice the claimed invention" (page 5, paragraph 4). In response to the issue that coelenterazine is toxic to cells, Applicant states, "coelenterazine is not included during cell culture" (page 5, paragraph 5). Applicant further states, "coelenterazine is not widely known in the art as toxic" and therefore "it would be apparent to one of skill in the art that any effect seen on cell proliferation following the teaching of the present invention would be due to the test agent" (page 6, paragraph 1). Applicants argue, "[m]ethods of collection of light are well known in the art" and "[a]s such, one of skill in the art would be able to practice the present invention without undue experimentation" (page 6, paragraph 2). Applicants also state, "the Examiner's attention is respectfully drawn to the fact that the present invention is not intended for therapeutic use, but as a screening method" (page 6, paragraph 3). Accordingly, Applicant states that "the independent claims of the present invention have been amended to claim '[a]n *in vitro* method'" (page 6, paragraph 3). In regard to the issue that the toxicity of coelenterazine may mask the effect of the agent upon the cells, Applicant argues, "the toxicity of coelenterazine, even if amplified by an additional agent, is not relevant, as that toxicity would not affect proliferation" (page 7, paragraph 1). Finally, Applicant remarks that the specification teaches a relationship between a change in light emission and a change in cell proliferation and then cites references that allegedly demonstrate that the relationship is also well known in the art (pages 7 and 8).

In response to Applicants remarks, it is first noted that though the preamble of claims 1, 18, and 31 has been amended to recite the limitation "[a]n *in vitro* method", while the claims no longer encompass a method in which the cells in and of a subject's body are contacted with the agent, the claims still read on a method comprising contacting whole, live cells in isolation of the subject's body with an agent. On the other hand, claim 63, which has not been amended to recite the limitation, still reads on an *in vivo* or an *in vitro* method. Furthermore, the specification teaches, "[t]he cells containing a Renilla luciferase are cultured under conditions that allow expression of Renilla luciferase. The luciferase activity can then be measured *in vivo* or *in vitro* [...] by providing the cell culture with the substrate coelenterazine" (underlining added) (paragraph bridging pages 19 and 20, now amended). Thus, in view of the disclosure, it is apparent the specification teaches that coelenterazine can be added during cell culture, a fact that directly contradicts Applicant's assertion in the remarks that "coelenterazine is not included during cell culture". As stated in the previous Office Action, the methods using intact cells are not exemplified in the specification. Furthermore, apart from the very brief disclosure in the paragraph bridging pages 19 and 20, there is no other guidance in the specification that would serve to teach one to practice the claimed method using intact and viable cells. In addition, the previous Office Action referenced the teachings of Dubuisson, et al to demonstrate that coelenterazine is toxic to cells and that the toxicity of coelenterazine is amplified in the presence of certain other agents. The specification provides insufficient guidance with regard to this issue, however. In particular, the specification does not teach how the effects of coelenterazine can be distinguished from the effects of the agent suspected of modulating cell proliferation. In view of the teachings of Dubuisson, et al and in the absence of sufficient guidance and exemplification of the claimed methods, one skilled in the art would not be able to practice the invention commensurate in scope with the claims with a reasonable expectation of success without first performing undue experimentation. Applicant argues that the toxicity of coelenterazine would be insignificant, "as that toxicity would not affect proliferation"; however, this argument directly contradicts the teachings of Dubuisson, et al. Again, Dubuisson, et al teach that

coelenterazine is toxic to cells and therefore certainly affects cellular proliferation, the extent to which Dubuisson, et al measures (page 473, Figure 3). The fact that "coelenterazine is not widely known in the art as toxic", as Applicant remarks, is inconsequential to the examination of the invention. However, Applicant's remark that "it would be apparent to one of skill in the art that any effect seen on cell proliferation following the teaching of the present invention would be due to the test agent" is akin to suggesting that "what one doesn't know can't hurt him or her". In this instance, if the disclosure were to be considered enabling, one might practice the invention according to the teachings of the specification, but erroneously arrive at the wrong conclusion, which certainly suggests that the skilled artisan would not be able to practice the invention with a reasonable expectation of success.

In the remarks, Applicants refer to a fragment of a statement made in the previous Office Action, namely "the specification is silent as to how valid light emission data can be collected in practicing the claimed methods". In response, Applicants argue, "[m]ethods of collection of light are well known in the art" and "[a]s such, one of skill in the art would be able to practice the present invention without undue experimentation". However, the fragment of the statement is taken out of the context of the paragraph in the previous Office Action, which actually queried how valid light emission data could be collected when the specification does not teach a method for distinguishing the toxic effect of coelenterazine from the effects of the agent that is being screened in the practicing the claimed method. As stated in the paragraph above, this issue has not been satisfactorily resolved.

In response to Applicant's remarks pertaining to the amendment, it is appreciated that the amendment to claims 1, 18, and 31 alters the scope of the claims so that the claims no longer encompass a method in which the cells in and of a subject's body are contacted with the agent. However, as noted above, the claims still read on a method comprising contacting whole, live cells in isolation of the subject's body with an agent. Nevertheless, the amendment to claims 1, 18, and 31 in part resolves the issue with regard to the toxicity of coelenterazine and whether or not coelenterazine can safely be administered to a subject in order to practice the claimed methods. However, also as

noted above, claim 63 is not currently limited to an *in vitro* method and therefore with regard to claims 63-68, this issue remains.

In response to Applicant's final remarks, exemplification of the claimed method is not commensurate in scope with the claims. The art is highly unpredictable, as evidenced by the teachings of Cree. Therefore, in the absence of exemplification that is commensurate in scope with the claims, one skilled in the art would not be able to practice the invention with a reasonable expectation of success without first performing undue experimentation. Jasmin, et al teach the requirement of "a strict correlation between in vivo bioluminescence and cell viability", but this strict correlation has not been established in the application. In view of the teachings of Dubuisson, et al, it is even more apparent that such a strict correlation necessarily need be established before one could practice the invention with a reasonable expectation of success. Thus, while there is certainly a relationship between cell viability and sensitivity to therapeutic agents, it does not necessarily follow that there is well known relationship between bioluminescence and cell viability and sensitivity to therapeutic agents. The correlation of bioluminescence and cell viability and sensitivity to therapeutic agents can only be established empirically and cannot be extrapolated from the teachings of the specification. Finally, it is noted that other issues were raised in the previous Office Action, which were not addressed in Applicants remarks.

While given full and careful consideration, in view of the preponderance of evidence, Applicant's arguments have not been found persuasive. Therefore, the rejection of claims 1-47 and 63-68 under 35 USC § 112, first paragraph for the reason set forth in the previous Office Action is maintained.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-47 and 63-68 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap

between the steps. See MPEP § 2172.01. The omitted steps are set forth in section 7 of the previous Office Action.

Applicant traverse the rejection of claims 1-47 and 63-68 under 35 USC § 112, second paragraph for the reason set forth in section 7 of the previous Office Action. Applicant's arguments have been fully and carefully considered but have not been found persuasive.

Applicant argues, "the claims do not omit essential steps" (page 9, paragraph 2). Applicant contends that the steps that the Examiner alleges to be essential are "not required for the practice of the present invention" (page 9, paragraph 2). Furthermore, Applicant states, '[a]s coelenterazine is hydrophobic, it may penetrate the cells without the assistance of a detergent to make the cell membrane permeable" (page 9, paragraph 2). Applicant refers to other methods of determining the viability of intact cells, which assays do not require the cells to be lysed.

In response to Applicant's arguments, firstly, it is noted that the specification does not teach, "[a]s coelenterazine is hydrophobic, it may penetrate the cells without the assistance of a detergent to make the cell membrane permeable". Secondly, consideration of well-known methods for determining the viability of intact cells, which do not require the cells to be lysed, is not seemingly germane to the examination of the present invention. Contrary to Applicant's assertion, the disclosure that "other methods of screening cells are available and are known to those of skill in the art" does not alter the fact that essential steps have been omitted in the claimed processes, which Applicant regards as the invention.

Furthermore, despite Applicant's argument, it is noted that the amendment to claims 1 and 31, which presently recite "comparing the light emission data from the cell in the presence of the agent to the light emission data from the cell in the absence of the agent", has in effect added one of the steps alleged by the Examiner to be essential to the claimed process, but which was omitted in the original claims. In other words, as amended, there is an obvious inference in claims 1 and 31 that light emission data must be collected from samples in the presence and absence of the agent; otherwise, one

could not compare the light emission data from the cell in the presence of the agent to the light emission data from the cell in the absence of the agent.

Applicants assert that a step in which the substrate coelenterazine is added to the samples is non-essential. However, certainly the substrate is as essential to the claimed process as the enzyme, namely luciferase, which activates the substrate, which, in turn, emits light. In fact, if the steps alleged by the Examiner in the previous Office Action to be essential are, in fact, "not required to practice the present invention", as Applicant argues, how can light emission be measured in the absence of emitted light.

With regard to claims 63-68, Applicants assert that a step in which the light emission data collected from cells in the presence and absence of the agent is non-essential. Paradoxically, it is noted that both claims 1 and 31 recite a step in which the light emission data collected from the cells in the presence and absence of the agent is compared; therefore, by its inclusion alone, this particular step is construed to be an essential step, which is required to the practice of the claimed process. Nevertheless, with regard to claim 63, since Applicant asserts that a comparison step is not essential to the claimed process, the question is, how can one practice the method without comparing the data acquired in the presence and absence of the agent and still successfully determine the susceptibility of the cells to the agent. Certainly the specification does not provide the guidance that would be necessary to do so.

Finally, Applicant asserts that it is not necessary to lyse the cells. As stated in the previous Office Action, however, the specification does not exemplify a method wherein the cells are not lysed or in which cell lysates are not used to determine the luciferase activity in a sample so acquired from the cells. There is insufficient guidance in the specification to practice the claimed method using intact cells. The only example provided is one in which the cells are lysed; therefore, the preparation of cell lysates is considered to be essential to the practice of the claimed methods, as there is no adequate teaching or example to suggest otherwise. This issue is also addressed in the grounds of the rejection of the claims under 35 USC § 112, first paragraph.

In summary, Applicant's arguments have been fully and carefully considered but for the reason set forth in the paragraphs above have not been found persuasive.

11. Claims 1-47 and 63-68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The grounds of rejection are set forth in section 8 of the previous Office Action.

Applicant traverses the rejections of claims 1-47 and 63-68 under 35 USC § 112, second paragraph for the reason set forth in section 8 of the previous Office Action. Applicant's argument has been fully and carefully considered, but has not been found persuasive.

With respect to the grounds of rejection of claims 1-17, Applicant argues, "[t]he use of the term 'an agent' in line 1 [of claim 1] is part of the preamble of the claim. Generally, a preamble is not considered limiting to a claim unless it breathes life and meaning into the claim. (See MPEP 2111.02)" (page 9, paragraph 5). Applicant further states, "[i]n the present invention, the claim following the transitional phrase 'comprising' stands alone. It is therefore unnecessary for the term 'an agent' in line 1 to serve as an antecedent basis for the use of 'an agent' in line 3" (page 9, paragraph 5). With regard to the rejection of claims 18-30, 31-47, and 63-68, Applicant states that for the same reason the use of the indefinite article in claims 18, 31, and 63 is acceptable. Therefore, Applicant asserts that the claims are not indefinite.

In response to Applicant's argument, it is noted that excerpts of MPEP § 2111.02 read as follows:

> "[A] claim preamble has the import that the claim as a whole suggests for it." Bell Communications Research, Inc. v. Vitalink Communications Corp., 55 F.3d 615, 620, 34 USPQ2d 1816, 1820 (Fed. Cir. 1995). "If the claim preamble, when read in the context of the entire claim, recites limitations of the claim, or, if the claim preamble is necessary to give life, meaning, and vitality' to the claim, then the claim preamble should be construed as if in the balance of the claim." Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165-66 (Fed. Cir. 1999). See also Kropa v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).
>
> Any terminology in the preamble that limits the structure of the claimed invention must be treated as a claim limitation. See, e.g., Corning Glass Works v. Sumitomo Elec. U.S.A., Inc., 868 F.2d 1251, 1257, 9 USPQ2d 1962, 1966 (Fed. Cir. 1989).

> The claim preamble must be read in the context of the entire claim. The determination of whether preamble recitations are structural limitations or mere statements of purpose or use "can be resolved only on review of the entirety of the [record] to gain an understanding of what the inventors actually invented and intended to encompass by the claim." Corning Glass Works, 868 F.2d at 1257, 9 USPQ2d at 1966. If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction. Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999). See also Rowe v. Dror, 112 F.3d 473, 478, 42 USPQ2d 1550, 1553 (Fed. Cir. 1997).

In view of the above excerpts of § 2111.02, the Examiner wonders if Applicant would still argue that the body of each claim in the instant application "stands alone". For example, would a claim to a method for determining the effect of an agent *be* a method for determining the effect of the agent, when the method does not comprise a step of "determining the effect of the agent".

Ironically, it is noted that in response to the previous Office Action Applicant amended the preamble of claims 1, 18, and 31 to recite the phrase "an *in vitro*". Should the claims' preambles be given no import since Applicant argues that the preambles do not limit the subject matter of the claims? In the instant application, if the recitations of the preambles of the claims are viewed as significant, then because the claims would no longer read on *in vivo* methods, the amendment to the claims could obviate part of the basis of rejection of claims 1-47 under 35 USC § 112, first paragraph for the reason set forth in the previous Office Action. If, however, the preambles are not given import, as Applicant apparently wishes, the recitations in the preambles of the clams should not to be considered limitations. Nevertheless, in the latter situation, while the preambles' recitations would not be considered limiting, the claims would still be indefinite because though the preamble is not given import, the preamble of a claim is not independent of the body of the claim. Therefore, in a claim containing a preamble, the language of the body of the claim must at least be congruent with the language of the preamble to avoid confusion in interpreting what subject matter Applicant regards as the invention. Hence, the claims in the instant application are unclear and indefinite because the language of the bodies of the claims and the language of the preambles of the claims is incongruent.

For this reason, though Applicant's argument has been fully and carefully considered, the rejection of claims 1-47 and 63-68 under 35 USC § 112, second paragraph for the reason set forth in section 8 of the previous Office Action is maintained.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1-47 and 63-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cree (*Methods in Molecular Biology* **102**: 169-177, 1998) in view of Virta, et *al (Antimicrobial Agents and Chemotherapy* **38**: 2775-2779, 1994), Edinger, et al (*DRU* **1**: 303-310, 1999), Prosser, et al (*Critical Reviews in Biotechnology* **16**: 157-183, 1996), and further in view of US 5,292,658 A, and US 6,171,808 B1, all references of record, for reason of record.

Applicant traverses the rejection of claims 1-47 and 63-68 under 35 USC § 103(a) for the reason set forth in section 10 of the previous Office Action, which is reiterated above. Applicant's arguments filed in Paper No. 8 have been fully considered but they are not persuasive.

Applicant argues, "[n]one of the references cited allegedly rendering the present invention obvious teach or suggest that the effect of an agent on cell proliferation may be tested via measurement of light emission using Renilla luciferase" (page 11, paragraph 2). Applicant remarks that Cree, Virta, et al, and Edinger, et al do not disclose a method for determining cell viability based upon measuring luminescence produced by *Renilla* luciferase page 11, paragraphs 2-4). Applicant further remarks, "[t]he teachings of the Prosser reference and U.S. Pat. Nos. 5,292,658 A and 6,171,809 B1 cannot overcome the deficiencies of the Cree, Virta, and Edinger references" (page

11, paragraph 5). Applicant summarizes, "[n]one of the cited references, alone or in combination, teach or suggest all of the claimed aspects to the present invention" (page 11, paragraph 6).

In response to Applicant's argument, it is noted that claims 1-47 and 63-68 are rejected under 35 USC § 103(a) in as being unpatentable over Cree in view of Virta, et al, Edinger, et al and Prosser, et al and in further view of US 5,292,658 A and US 6,171,808 B1. Accordingly, the answer to Applicants apparent query in the summarizing statement is that the invention is unpatentable over the *combination* of the teachings of the cited references. In this regard, it is noted that Applicant addressed each of the cited references individually, but one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Furthermore, in direct response to Applicant's argument that the teachings of Prosser, et al and US Patent Nos. 5,292,658-A and 6,171,809-B1 cannot overcome the deficiencies of the primary references, the test for obviousness is not whether the features of the secondary references may be bodily incorporated into the structure of the primary references; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Thus, while having been fully and carefully considered, Applicant's arguments are not found persuasive. Accordingly, the rejection of claims 1-47 and 63-68 under 35 USC § 103(a) for the reason set forth in the previous Office Action is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

14. Claims 18-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 18-30 are vague and indefinite because claim 18 recites the term "a corresponding change". Recitation of the term renders the claims vague and indefinite because it is unclear to what subject matter the change corresponds. Furthermore, it is unclear how that subject matter is required to correspond to the change. Accordingly, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. Amending claim 18 to delete "corresponding" can obviate this rejection.

Conclusion

15. No claims are allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (703) 305-3008. The examiner can normally be reached on Monday-Thursday, alternate Fridays, 8:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

DONNA WORTMAN
PRIMARY EXAMINER

slr
October 30, 2001